MEMORANDUM

TO: Members, Manufacturing Subcommittee of the Advisory Committee for Pharmaceutical Science

FROM: Ajaz S. Hussain, Ph.D.
Deputy Director, Office of Pharmaceutical Science, CDER, FDA

Date: August 22, 2003

RE: Manufacturing Subcommittee Meeting - September 17, 2003

Dear Subcommittee Members and Invited Guests,

We look forward to meeting you on 17 September 2003 to continue discussions on two important scientific topics we introduced to you at the previous meeting, i.e., *Manufacturing Science* and *Risk Based Regulatory Decisions*. The discussions on 17 September 2003 will first focus on approaches for assessing *Quality by Design* and then on approaches for *risk based regulatory decisions* for CMC post approval change assessments and cGMP inspections. Prior to discussing these topics we have invited Dr. Tobias Massa to provide you a summary report of the FDA/PQRI workshop entitled "A Drug Quality System for the 21st Century" that was held in Washington DC in April 2003. Following this report Dr. Woodcock will share with you her thoughts on the elements that constitute a definition of *pharmaceutical quality*.

Topic #1: *Quality by Design*

We believe that a focus on *quality by design* provides opportunities to improve the usefulness of relevant product and process knowledge during regulatory decision making — without affecting a manufacturer's development program. These opportunities are identified in many elements of the Desired State for Manufacturing we discussed with you at the previous meeting, i.e.,

- Product quality and performance are ensured through the design of effective and efficient manufacturing processes
- Product and process specifications are based on a mechanistic understanding of how formulation and process factors affect product performance
- Continuous *real time* quality assurance
- Relevant regulatory policies and procedures are tailored to accommodate the most current level of scientific knowledge
- Risk-based regulatory approaches recognize
    - the level of scientific understanding of how formulation and manufacturing process factors affect product quality and performance and

- the capability of process control strategies to prevent or mitigate the risk of producing a poor quality product

To initiate discussion on *quality by design* we have requested:

- Dr. G. K. Raju of this subcommittee to articulate how one can achieve and gauge or measure *quality by design.*
- Dr. Norman Schmuff a team leader in our Office of New Drug Chemistry to provide a CMC review perspective on the challenges is assessing *quality by design* with the current level of pharmaceutical development information contained in submissions.
- Mr. Gerry Migliaccio to expand further on previous presentation to the subcommittee on the topic of *manufacturing science* to address and propose approaches for sharing the right level of pharmaceutical development knowledge to facilitate regulatory assessment of *quality by design*.
- A Generic Industry (GPhA) perspective and proposal on this topic
- Prof. Ken Morris (University of Purdue) to provide an academic perspective and proposal on this topic.
- Ajaz Hussain and Joe Famulare will provide a regulatory CMC review and cGMP compliance perspectives, respectively.

Committee discussions will follow these presentations. We request the subcommittee to provide us their suggestions and recommendations on the following aspects:

- Articulate a clear description of the term *quality by design*
- Identify the type of information and knowledge most useful to assess *quality by design*
- Regulatory approach for assessment of pharmaceutical development knowledge to maximize its value without impacting drug development

Topic #2: Relationship between *Quality by Design* and *Risk Based Regulatory Scrutiny*

In this discussion we seek subcommittee recommendations on ways to link the concept of *risk based regulatory scrutiny* to *quality by design*.

To initiate these discussions we have requested Dr. Collin Gardner to further expand on his presentation ("Make - Your-Own-SUPAC") at the previous subcommittee meeting to discuss scientific approaches for risk based regulatory CMC review process. Dr. Greg Guyer has been invited to share his perspectives on risk based cGMP inspections. Dr. Guyer is the lead for ICH topic on risk based cGMPs.

As background information to support these discussions we have included in the background material:

- Draft Guidance for Industry: Drug Product, Chemistry, Manufacturing, and Controls Information
- ICH Concept paper and proposals on pharmaceutical development
- Transcripts of past ACPS meetings on risk based CMC review

- FDA/PQRI Workshop reports
- The draft guidance on PAT is currently under review and will be available prior to the meeting. We will make this available to the subcommittee as soon as it is publicly available